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Introduction.—The literature of this neglected phase of cytology is scanty, and has been reviewed in the previous papers of this series.[1] In summary, Brisseau-Mirbel (1802 and 1809) pictured in three dimensions what he considered to be typical cells of vegetable parenchyma; and Kieser (1815 and 1818), recognizing that Mirbel had drawn truncated rhombic dodecahedra, adopted and exploited the idea, believing it to rest on a firm physical basis. But cells are so irregular that biologists took only a waning interest. In D'Arcy W. Thompson's remarkable book, described by its author as "all preface—an easy introduction to the study of organic Form by the methods which are the common-places of physical science"—the question of the shape of cells is again introduced, for physicists had meanwhile provided *a priori* reasons for assuming cells to be tetrakaidecahedral. Yet balls of putty compress into dodecahedra, and Professor Thompson, influenced apparently by the 12-rayed stars of Juncus pith, was inclined toward the older view.

Knowing that the actual shape of certain cells could be determined by laborious application of the wax-plate reconstruction method, I began what is now more than a ten years' study of cell forms. The initial question has been definitely answered. Tissues are not composed of rhombic dodecahedral cells, truncated or otherwise, for those shapes have characteristic tetrahedral angles which cells avoid. In a mass of cells of approximately uniform size, the average cell has 14 faces of contact with its neighbors: it is a tetrakaidecahedron. Data in proof of this are gathered in Table I.

[1] Lewis, F. T. The typical shape of polyhedral cells in vegetable parenchyma and the restoration of that shape following cell division. Proc. Amer. Acad., 1923, vol. 58, pp. 537–552.

—— A further study of the polyhedral shapes of cells. I. The stellate cells of *Juncus effusus;* II. Cells of human adipose tissue; III. Stratified cells of human oral epithelium. Proc. Amer. Acad., 1925, vol. 61, p. 1–34.

As previously published, 100 cells of elder pith, taken at random, have the number of contacts shown in the top line of the table, with an average of 13.97 facets. One hundred fat cells, also previously reported, are in the line below, with an average of 14.01 facets. Fifty precartilage cells of the tadpole, here presented for the first time, complete the tabulation; they average 13.9 facets. Altogether the 250 cells have an average of 13.97 facets. Not only from this counting of actual faces, but from geometrical considerations to be explained presently, we conclude that cells massed in tissues are primarily tetrakaidecahedra.

TABLE I.

No. of Facets	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Elder pith 100 cells	1	1	2	0	2	8	8	21	16	19	10	2	3	6	1	
Human fat 100 cells				2	4	5	15	13	20	15	17	4	2	2	1	
Precartilage 50 cells				1	1	4	9	8	10	7	3	3	2	1	0	1
Total	1	1	2	3	7	17	32	42	46	41	30	9	7	9	2	1

No longer should the cautious histologist evade this issue by using the term 'polyhedral.' Schaffer, quoting the observation that fat cells have from 9 to 20 facets, comments that it is idle to pursue the subject further—es wohl müssig erscheint, die Zahl der Kontaktflächen näher zu erörtern.[2] But when Nemiloff can write that "viele beschriebenen histologischen Strukturen sind sozusagen „Gottesmutterhaar", welches nur Gläubige sehen können,"[3] any feature of cells definite enough for mathematical expression seems worth investigating. What causes underlie the tetrakaidecahedral shape?

The essential requirement for the production of 14-hedra.—It is quite evident that tetrakaidecahedra are the three-dimensional expression of forces which produce the characteristic patterns of epithelial mosaics. Since it is easier to deal with plane surfaces than with solids, several preliminary studies have been made of the patterns of simple epithelium in surface view.[4] In such mosaics, as is well known,

[2] Schaffer, J. Die Stützgewebe. Hdb. d. mikr. Anat. d. Menschen, herausgegeben von W. v. Möllendorff, Bd. 2, Tl. 2, 1930, p. 75.

[3] Nemiloff, A. Über einige Widersprüche in der heutigen Anatomie und Histologie. Anat. Anz., 1932, Bd. 73, p. 362.

[4] Lewis, F. T. The effect of cell division on the shape and size of hexagonal cells. Anat. Rec., 1926, vol. 33, p. 331–355.

usually three cells meet at every corner. Exceptionally 4-rayed vertices occur, and sometimes frequently. The effect which they have upon the pattern is definite and can be mathematically expressed. But at the outset it may be assumed that only 3-rayed vertices occur. Then, if the mosaic entirely covers any solid body, whether a sphere, a cucumber-shape, or the complex form of an embryo, its polygons will have twelve less sides than if they were all hexagons.[5] This loss of sides is in connection with the rounded form of the body, and a deficiency of six would be expected at either end of the cucumber. If the polygons are small and there are thousands or millions of them, their average number of sides in any little flat area will be exactly six, except as chance may lead to such incidents as including a pentagon in the patch and excluding the balancing heptagon, or to including some of the polygons contributing to the deficiency of twelve sides as just mentioned.[6]

Thus it comes about that if many central points or nuclei are scattered at random over a flat surface, which is then subdivided into polygons so that each contains a nucleus, and the polygons invariably form 3-rayed vertices with their neighbors, the resulting mosaic will duplicate the cellular pattern in consisting of polygons with an average of close to six sides. Hence it may be inferred that hexagonal cells are not circles compressed into hexagons: they arise from the subdivision of a syncytial or plasmodial mass, by the formation of walls separating each nuclear territory from those that adjoin it. *Cell division is essentially a continuation of this process.* Before any walls have formed, nuclear division is tantamount to cell division; but after the walls have appeared, nuclear division merely produces bi-

Lewis, F. T. The correlation between cell division and the shapes and sizes of prismatic cells in the epidermis of Cucumis. *Ibid.*. 1928, vol. 38, p. 341–376.

—— A volumetric study of growth and cell division in two types of epithelium,—the longitudinally prismatic epidermal cells of Tradescantia and the radially prismatic epidermal cells of Cucumis. *Ibid.*, 1930, vol. 47, p. 59–99.

—— A comparison between the mosaic of polygons in a film of artificial emulsion and the pattern of simple epithelium in surface view (cucumber epidermis and human amnion). *Ibid.*, 1931, vol. 50, p. 235–265.

—— Mathematically precise features of epithelial mosaics: observations on the endothelium of capillaries. *Ibid.*, 1933, vol. 55, p. 323–341.

[5] There would be a further deduction of two sides for every 4-rayed vertex, of 4 sides for every 5-rayed vertex, etc.

[6] The mathematical conditions requisite for finding an average of precisely six sides in a given patch of cells have been formulated by W. C. Graustein, Annals of Mathematics, 1931, vol. 32, p. 149–153. The deduction of twelve sides in the mosaic covering a solid, or lining a cyst, is explained by the writer in the Anatomical Record, 1933, vol. 55, p. 323–341.

nucleate cells, and cell division awaits the formation of the intervening partitions. The new cell walls, like the old, form 3-rayed intersections only, and therefore the cells continue to be, on the average, hexagonal. Intersections with more than three rays are unstable and consequently eliminated.

The instability of a quadruple intersection may be simply illustrated with a model, using four light elastic bands of equal length and thickness (the rubber 'elastics' for securing parcels). On a drawing-board make two lines crossing at right angles (though other angles serve as

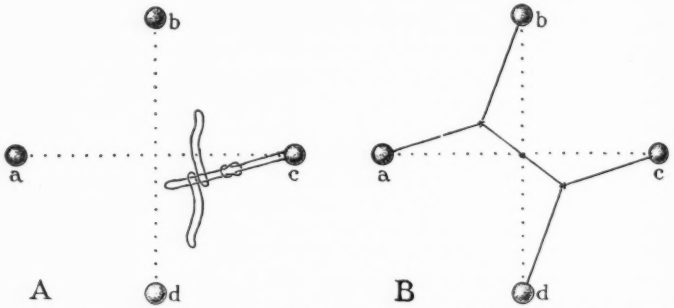


FIGURE 1. Arrangement of elastic loops to show the instability of a 4-rayed intersection.

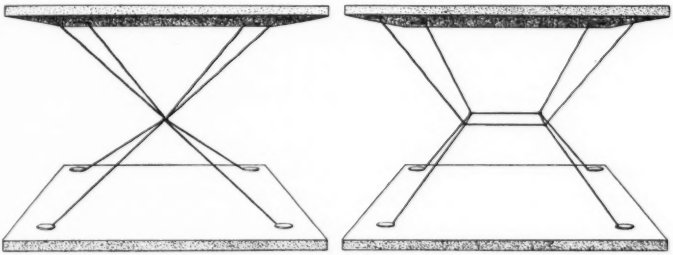
well), and along these lines insert four thumb tacks equidistant from the point of intersection. The distance chosen should be two or three times the length of the unstretched elastics. Join two of the elastics end to end making one of double length, and having slipped it through the other two (Fig. 1, A) stretch it from thumb tack *c* to *a*. The other elastics are placed around *b* and *d*. The four will not remain above the lines crossing at right angles, but will snap toward the position shown in Fig. 1, *B*, in which they are at rest with angles between them approximating 120°.[7] Professor P. W. Bridgman describes the situation as follows:

Four equal tensions are not in *stable* equilibrium when meeting at a common point. A very simple geometrical calculation shows that the total length of the heavy lines in Fig. 1, *B*, is less than that of the dotted lines. Hence according to the mechanical principle that a system seeks the configuration of

[7] The same thing may be beautifully shown in a moving picture of soap-bubbles rising over a plate glass surface, such as the author exhibited at the session of the Amer. Assn. of Anatomists in 1930. But the model with the elastic bands seems quite sufficient.

least energy, the configuration with the quadruple point will pass over into that with two triple points, provided the transition can be made. Opportunity for the transition is afforded by the slightest accidental disturbance. In other words, the system with quadruple points is in unstable equilibrium.

The quadruple point or four-rayed intersection, as it exists on the surface of a liquid polyhedron or cell, constitutes a tetrahedral angle. It is a corner of a cell where four of its facets meet at a point, instead of three. Like the 4-rayed intersection in the plane mosaic, it is unstable, and is commonly resolved into two triple points or trihedral



A B

FIGURE 2. Arrangement of elastic loops to show the instability of tetrahedral angles.

angles connected by a line or edge. This has been made very familiar by Plateau's wire cube dipped in soap solution. The directions of the forces involved are more clumsily but perhaps more clearly expressed by arranging elastics as in Fig. 2, *A*. Into each of two drawing-boards insert four thumb tacks at the corners of an 8-inch square, and invert one board over the other at a height of 8 inches. Stretch four elastics from the thumb tacks in the upper square to those in the corresponding corners of the lower square, and tie the four together at the central point, completing the arrangement in Fig. 2, *A*. If the elastics were connected with one another by films extending from the center to the thumb tack squares (but not crossing the squares diagonally) these films would bound six tetrahedral angles meeting at the central point. At the center there is a lateral stress tending to a different configuration. If instead of being tied together at the center, the elastics there pass through another and rather short elastic, they will stretch it into more or less of a square as seen in Fig. 2, *B*. Friction offers some resistance, but all the tetrahedral

angles are replaced by trihedral angles. Since the elastic skins of liquid drops—the cell membranes—act in this way, avoiding as a rule the unstable tetrahedral angles and 4-rayed intersections, it is inevitable that cells in masses shun the rhombic dodecahedral form, but a further condition must be met for an average of 14 facets.

The production of 14-hedra by the avoidance of tetrahedral angles and 4-rayed intersections.—That compliance with this requirement may yield tetrakaidecahedra is shown in a conventional diagram, Fig. 3.

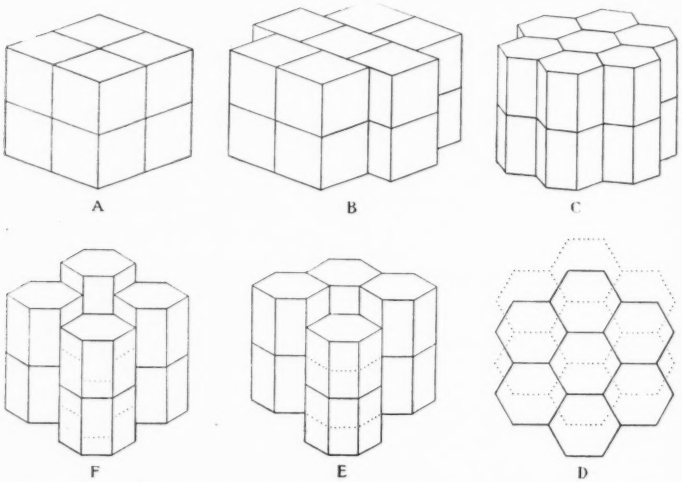


FIGURE 3. Diagram to show transformation of an aggregation of cubes into tetrakaidecahedra by the avoidance of 4-rayed intersections and tetrahedral angles.

Cubes (Fig. 3, *A*) have trihedral angles only, but they can not be arranged so as to avoid 4-rayed intersections without ceasing to be cubes, *i. e.* cells which are in contact with but six of their neighbors. If arranged as in Fig. 3, *B*, they avoid 4-rayed intersections in the horizontal plane but retain them in the vertical planes: they have become hexagonal 8-faced prisms. If the sides and angles of the hexagons are made equal, which is a change toward minimal surface expected in the more plastic animal tissues, Fig. 3, *B*, becomes *C*. There remain the 4-rayed intersections in the vertical planes.

If in an attempt to avoid these 4-rayed intersections, a single column is depressed by half the height of a prism, as in *E*, every 8-

faced prism in the depressed column acquires six additional facets by the bisection of its lateral facets, and becomes a tetrakaidecahedron. It presents, however, in its equatorial plane, six tetrahedral angles (two of which are fully exposed in the diagram). But this depression by half the height can not occur in alternate columns so as to make all the prisms 14-hedra. Depression of alternate rows by half the height makes them all dodecahedra, with two undivided vertical facets, which are on opposite sides of the prism. These two undivided facets retain their 4-rayed intersections above and below. The other four vertical facets are cut in halves transversely, forming eight quadrilaterals, separated by the undivided verticals into two groups of four each. Each group forms at its center a tetrahedral angle, and this angle is at the end of the line of 4-rayed intersection formed by the adjacent cells. This curious pattern was the norm postulated by Mirbel and Kieser.

An entire absence of the unstable tetrahedral angles and 4-rayed intersections, with walls so spaced as to avoid them to the maximum, occurs when the columns of prisms surrounding any given column are depressed alternately by one third and two thirds of the height of the prism (Fig. 3, *F*). There are then 14 faces per cell,—8 hexagonal and 6 quadrilateral. The cells are hexagonal in transverse and in vertical section. With all edges of the same length, the polyhedron becomes Kelvin's *orthic* tetrakaidecahedron, which divides space without interstices into uniform bodies of minimal surface.

The same result may be obtained, starting from the arrangement in Fig. 3, *C*, by shifting laterally the horizontal strata so that the central point in the base of any prism is over the mid-point of one of the sides of the prism beneath. The pattern of the superimposed tops and bases of the prisms becomes that shown in *D*. Each prism is in contact with four others below, four above, and six laterally. If all edges are made of the same length, it is again an orthic tetrakaidecahedron, but instead of presenting a top and basal surface as before, it is now oriented with an edge above and below.

It may be noted that when balls of such material as putty are in a pile, they settle into the hollows between their neighbors, so that when compressed, the relation of the superimposed layers (in a diagram corresponding with Fig. 3, *D*) is that of hexagons centered over the *angles* of the hexagons in the layer beneath. Each hexagon is then in contact with three above, three below, and six laterally. Compression thus yields dodecahedra, with six tetrahedral angles, radically different from the pattern of cells.

Polyhedra, formed around nuclei distributed at random, by enclosing them in mutually contiguous compartments which have trihedral angles only, and along whose edges three compartments invariably meet, will have an average of 14 facets.—After considering the exacting manner in which the cubes of Fig. 3 must be adjusted to yield orthic tetrakaidecahedra,[8] one is surprised to find that a random arrangement of polyhedra varying in their number of facets, but avoiding tetrahedral angles and 4-rayed intersections, will have the same average number of facets, namely 14. It can readily be shown that an assemblage of polyhedra, with the requisite trihedral angles and edges of triple intersection, can be constructed which shall *not* have an average of 14 facets, presenting either more or less as may be desired; yet with a *random* distribution of nuclei, it appears that the theorem, as stated in the caption of this paragraph, is correct. It must be left for others to provide a mathematical demonstration. We reach our conclusion as follows.

With certain qualifications, it has already been shown that the meshes of a net, limited to 3-rayed vertices, and formed around spots scattered at random over a plane surface, will be, on the average, hexagonal. Such patterns may be inscribed, for example, around raindrops, or stars in a simple constellation-chart. To resemble cellular mosaics or emulsions, the polygons should have no internal angles of more than 180°. Further, if a cellular mosaic is to be duplicated, the polygons should be mostly pentagons, hexagons, and heptagons. Greater and more frequent deviations from the hexagon are often seen in inorganic emulsions.[9] Finally, with a given set of points, one may draw triangular meshes or omit them altogether. None will be drawn, since triangular cells are infrequent.

With these considerations in mind, and wishing to know the number of facets in polyhedra of the cellular type formed around random nuclei, a series of 8-inch squares was drawn, in each of which 30 points were placed. These roughly followed some constellation pattern, with a single point in place of any close pair or cluster, and the arbitrary insertion of a point somewhere in any large empty space. The polygons with 3-rayed vertices inscribed around such nuclei ranged from quadrilaterals to octagons inclusive, with an average of 5.96 sides. Then the mosaics, which had been drawn on transparent paper,

[8] See also Proceedings, vol. 61, p. 25, for a diagram where, by *tour de force*, solid spheres are arranged to yield 14-hedra on compression: with comments on the same in Anat. Rec., vol. 50, p. 238–239.

[9] *Cf.* Anat. Rec., vol. 50, p. 244 and 241.

were successively superimposed, in the manner shown in Fig. 4. Wherever tetrahedral angles or 4-rayed intersections occurred, the boundaries of the polygons were shifted to avoid such instabilities. It was then found that the polygons of a given layer were, on the average, in contact with 4 others in the layer above, and 4 in the layer below, making them altogether 14-hedra. Without reconstruction, but quite as definitely as if modeled in wax, the number of facets of

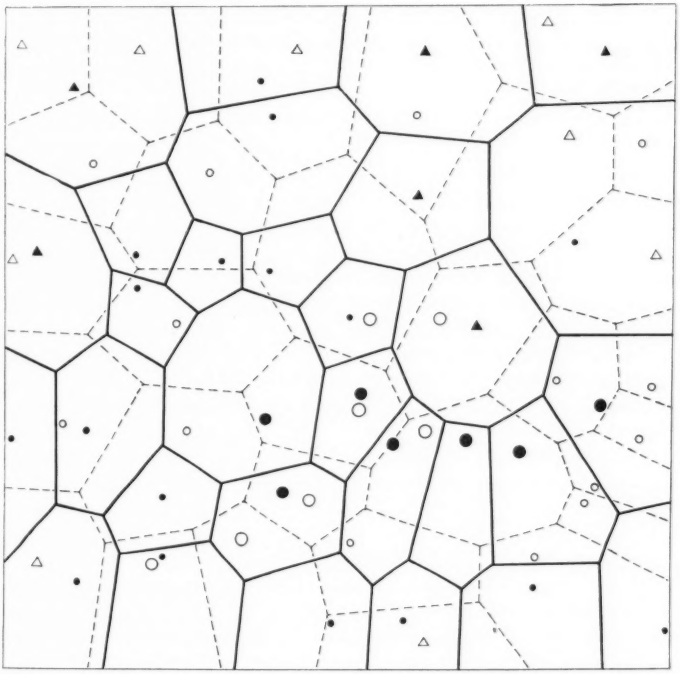


FIGURE 4. In heavy lines, polygons with 3-rayed intersections formed around 30 points distributed in a square at random. In lines of dashes, another set of polygons similarly formed around 30 other random points. (These random points are free renderings of Ursa major and minor, with the triangular points arbitrarily added.) The superimposed patterns, adjusted to avoid 4-rayed intersections and tetrahedral angles, include 27 cells completely within the square, having an average of 5.93 sides, and an average of 4.2 contacts with cells in the adjoining layer.

the individual polyhedra could be counted. It was found that 100 of them had from 9 to 21 facets (Table II) with an average of 14.11. They are quite comparable with the hundred fat cells, repeated from Table I. If, then, a haphazard distribution of nuclei is sufficient to yield a tetrakaidecahedral tissue, we may expect to find it in cartilage, where as Holmes expressed it, the cells are scattered like "plums in a pudding."[10]

TABLE II.

No. of Facets	9	10	11	12	13	14	15	16	17	18	19	20	21
Schematic polyhedra around 100 random centers	1	6	6	10	22	21	11	4	8	3	4	3	1
Human fat, 100 cells	2	4	5	15	13	20	15	17	4	2	2	1	

The form of cells in precartilage.—In view of the foregoing conclusion that cells properly formed around random nuclei will have an average of 14 facets, it seems indeed 'idle' to reconstruct precartilage cells and find that they too are tetrakaidecahedral. But it was a preliminary inspection of the models of such irregular cells that led to the generalization, and there are properties of the cells other than their number of facets which will be revealed by this study.

A single tadpole of the common toad (*Bufo lentiginosus*) supplied all the cartilage cells reconstructed. Preserved presumably in formalin, this tadpole measured 25 mm.: its hind legs were nearly 3 mm. long and the front legs were not yet free. A portion of the head was cut in serial sections 3 μ thick, by Mr. A. G. Mahurin, using a Minot precision microtome, and they were stained with iron haematoxylin and Orange G. Individual cells, readily identified, extended through 7 to 15 sections, usually about 10. They were drawn, with projection apparatus, at a magnification of 1330 diameters; and after their contacts had been determined, certain of them were reconstructed by the wax-plate method. I am indebted to Ethel S. Lewis for making all the models. They have been drawn, also with great skill, by Mr. F. Schuyler Mathews.

The portion of the mandibular cartilage shown at *a* in Fig. 5 was chosen for special study, and all the models were made from it. Its cell pattern is seen in Fig. 6. Avoiding the small cells at the periphery and those in immediate relation with them, a count of the intercellular surfaces of 25 cells was made, and the average number of faces per cell

[10] Holmes, O. W. The human body, Atlantic Almanac, 1869, p. 48.

was 14.08. For 25 cells from the interior of the cranial cartilage (Fig. 5, *b*) the average was 13.7, making the average for 50 cartilage cells, as listed in Table I, 13.90.

The cell pattern of precartilage (Fig. 6), except for higher magnification, has been drawn in the same manner as the fat cells and elder pith of the earlier studies (*cf.*, respectively, these Proceedings, vol. 61, p. 20 and vol. 58, p. 543). On comparing these figures, one thinks of Leydig's comment that cartilage may look like fat 'to a hair.' "Betrachtet man z. B. die Kehlkopfknorpel der Nager (Ratte), so glaubt man nicht Knorpel vor sich zu haben, sondern echtes Fettgewebe; erst genaueres Zusehen belehrt, dass ein Knorpel vorliege. . . ."[11]

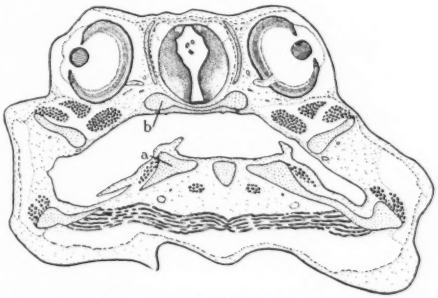


FIGURE 5. Section of the head of a toad tadpole; at *a* and *b*, the precartilages studied. × 15 diam.

But when these two tissues are compared with vegetable parenchyma, even though an eminent cytologist has noted a "striking resemblance," we find a more striking difference. In the elder pith, but not in the other two, there tends to be an orderly arrangement in columns, with a vertical repetition of queerly sectioned corners and a lateral dovetailing of the polygons. When modeled, the elder cells alone are commonly oriented with a surface above and below: frequently they have two tiers of lateral facets, with occasionally the alternation of quadrilaterals and hexagons in a manner suggestive of Kelvin's orthic tetrakaidecahedra. In fat and precartilage, with the same average number of facets, the cells seem piled in lawless confusion. This is shown in the model, Plate I.

The model includes 14 of the cells marked with numerals in Fig. 6. With them are two other entire cells (16 altogether), and a portion of

[11] Leydig, F. Lehrbuch der Histologie. 1857, p. 34.

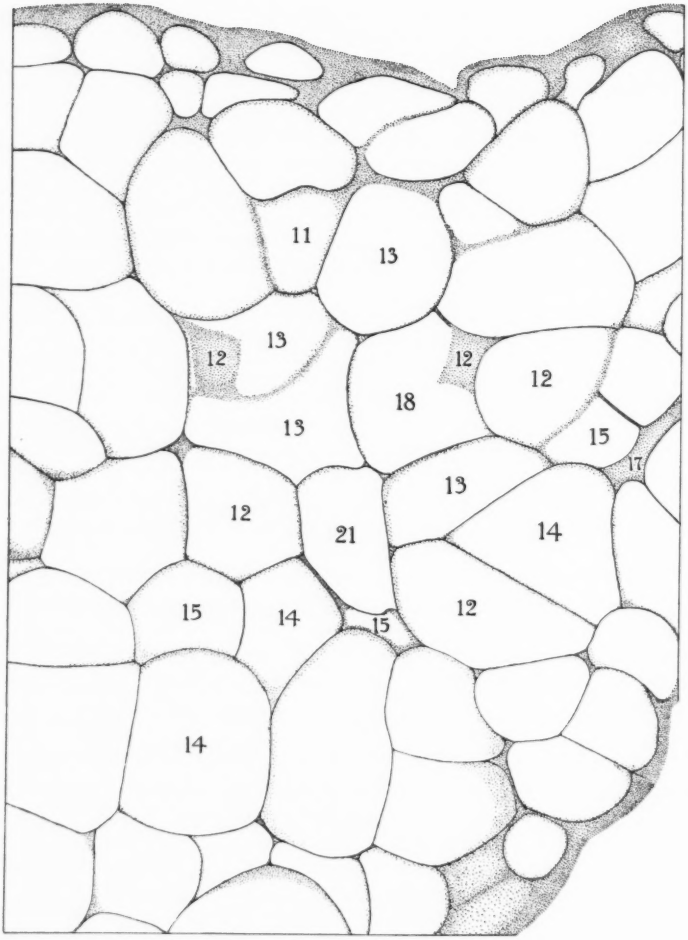


FIGURE 6. Section of the mandibular precartilage of a toad tadpole of 25 mm. The numerals in certain cells indicate their number of contacts with other cells. × 600 diam.

a seventeenth which was defective in its hidden aspect. The 16 complete cells, with an average of 14.1 facets, range from 12 to 21 facets each. These facets vary from triangles to nonagons. They form 312 trihedral angles and 15 tetrahedral, nearly 5 per cent. being of the unstable form. In such a group one may well ask whether there is any semblance of order. Most decidedly there is, as will appear from the following considerations.

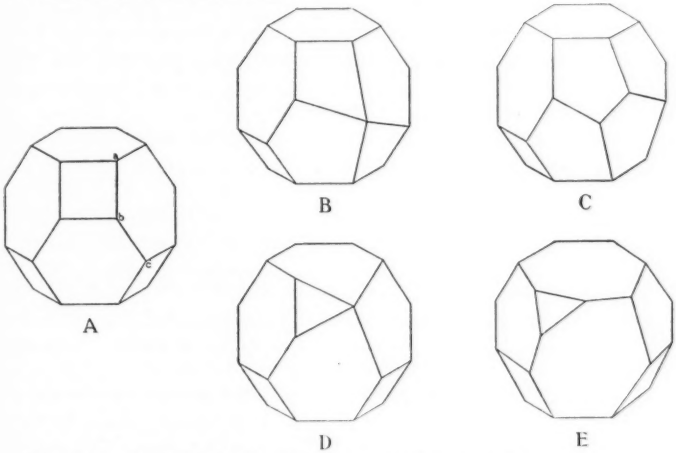


FIGURE 7. Irregular tetrakaidecahedra (*B–E*) derived from the regular or orthic tetrakaidecahedron, *A*.

The orthic 14-hedron (Fig. 7, *A*) has 8 hexagonal and 6 quadrilateral facets, which together have 72 sides (36 edges, each common to two polygons). Let the edge *bc* between two hexagons be reduced to a point, and a tetrahedral angle is formed (Fig. 7, *B*): there are then 14 facets with 70 sides and one tetrahedral angle. Then, if between the irregular quadrilaterals of Fig. 7, *B*, an edge develops, making them pentagons (Fig. 7, *C*), we again have a 14-faced cell with 72 sides and no tetrahedral angles. Or, in Fig. 7, *A*, let the edge *ab*, between a quadrilateral and a hexagon, be reduced to a point (Fig. 7, *D*) and we have another 14-faced body with 70 sides and a tetrahedral angle. If, then, an edge develops extending from the triangular face to the pentagon (Fig. 7, *E*), thereby producing two heptagons and eliminating the tetrahedral angle, there is once more a 14-faced body with trihedral angles only, and facets totaling 72 sides.

Thus it is observed that any combination of polygons which covers the surface of a 14-hedron and makes trihedral angles only, will have a total of 72 sides, and that there will be a deduction of two sides for every tetrahedral angle. The cartilage cells are formed under this law, which as Professor W. C. Graustein informs me, is readily deducible from Euler's famous formula. If F is the number of faces of a polyhedron; V, its number of vertices or corners; and E, the number of edges; then $F + V - E = 2$. Euler's theorem is cited in Thompson's *Growth and Form* (1917, p. 385 and 484), but its wide application to cell shapes and mosaic patterns has generally been unsuspected. In a previous paper,[12] and in what follows, we deal only with the cytological phases of Euler's comprehensive scheme which assures us that the empirical deductions from the study of cartilage cells are mathematically sound.

Plate II, fig. 17, shows a 14-hedral precartilage cell with 3 triangular facets, 3 quadrilateral, 2 pentagons, 3 hexagons, 1 heptagon and 2 octagons, and no tetrahedral angles. There are of necessity 72 sides (36 edges) and 24 corners, as in an orthic 14-hedron. Plate II, fig. 18, is another precartilage cell with 14 facets,—2 triangles, 5 quadrilaterals, 1 pentagon, 5 hexagons and 1 heptagon—but there are two tetrahedral angles, both of which appear in the drawing. This cell then has necessarily four less than the 72 sides of the orthic 14-hedron.

If, in Fig. 7, E, the triangular facet should become smaller till it disappeared, three edges would be lost: a 13-hedron would be produced, with facets having 6 less sides than the 14-hedron. Conversely if a triangular facet should be added to the orthic 14-hedron (Fig. 7, A) by truncating one of its angles, six sides would be added. In general it may be said that with trihedral angles only, when n is the number of facets, $6(n - 2)$ is their total number of sides. There is a deduction of two sides for every tetrahedral angle. The number of edges is $3(n - 2)$ with a deduction of one for every tetrahedral angle. The number of angles when all are trihedral, is $2n - 4$, and there is a deduction of one for every tetrahedral angle. These being geometrical necessities, actual examples are really superfluous. Pl. II, fig. 19, is a flattened misshapen precartilage cell with 13 facets. Its angles are all trihedral. There must be 22 of them, and the facets must have a total of $6(13 - 2)$ sides, or 66. This cell has 2 triangular facets, 3 each of quadrilaterals, pentagons, and hexagons, 1 heptagon and 1 octagon. Plate II, fig. 20, is a cell with 21 facets, and 2 tetrahedral angles. Its facets have 110 sides, being $6(21 - 2) - 4$. It has 36 angles, 34 being trihedral.

[12] Anat. Rec., 1933, vol. 55, p. 323.

Volume of precartilage cells.—It has previously been shown that the average area of the polygons in an epithelial mosaic varies with their number of sides, and in definite arithmetical progression.[13] We rather confidently expect the same to be true of the polyhedral cells in the interior of precartilage, yet this can be demonstrated only with far more extensive and more accurate data than are at hand. Modeling in wax at a magnification of 1330 diameters, or × 2,352,637,000, is not very precise. Variation in the size of cells of a given number of facets is clearly so extensive, that for a significant average many should be measured. However, the volumes of the twenty models of precartilage cells, determined by displacement, are shown in Table III.

TABLE III.

No of Facets	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Precartilage, 20 cells, × 1330 diam. Volume in cc.		25		25	30 50 50 55	30 35 45 55 60	50 55 55 80	60		75	60	75		80
Average Volume		25		25	45	45	60	60		75	60	75		80
Elder pith, 30 cells × 500 diam. Volume in cc.	30		55	65 65	45 55 65 75 100 125	60 80 85 90 90 95	70 80 95 140 140	80 95 105 120	120 130		175	175 295		
Average Volume	30		55	65	80	85	105	100	125		175	235		

Thirty cells of elder pith, the volumes of which in relation to their number of facets, have not previously been recorded, have been added in the table. Fragmentary as these data are, it seems clear that the average volume of polyhedral cells, under similar conditions within a mass, increases with the number of facets.

A more decided increment in volume per facet is found in conventional polyhedra, in which all edges are made of equal length. This accords with the fact that in a plane epithelial mosaic, whereas the average area of a polygonal cell increases with its number of sides, the increase is less than that of the corresponding regular polygons with sides of unit length. There is a tendency toward uniformity. The few-sided polygons and few-faceted polyhedra are larger than would be expected: the many-sided and many-faceted are smaller.

[13] Anat. Rec., 1928, vol. 38, p. 365; 1931, vol. 50, p. 258.

Of relatively little interest is the actual size of the precartilage cells. Calculated from the models, it is found to range from .000011 c. mm. to .000034 c. mm., with the 14-hedron averaging .000025 c. mm. The average human fat cell is 20 times larger; and the cell of elder pith, with an average volume of approximately .001 c. mm., is 40 times larger.

Cell division in precartilage cells.—One of the most significant observations in this ten years' study may be discounted as axiomatic, so patent and obvious it is—after attention has been called to it. In a plane mosaic, the inevitable result of the division of a polygonal cell by a wall which avoids 4-rayed intersections is to produce two daughter cells which together have four more sides than the parent, and to add one side to each of two adjacent cells. Every such division thus adds one cell and six sides to the mosaic. Given a mosaic of hexagons, division must introduce few-sided polygons and create many-sided. Even though subsequent divisions tend to correct this, they never perfectly succeed. The average number of sides of the dividing cells in an epithelial mosaic is found to be seven, but heptagons can not divide into two hexagons; nor are the cells at the end of the division plane always pentagons to be restored to hexagons. A variety of polygons in the mosaic, and of polyhedra in the mass, is the inevitable result of cell division, except under the ideal conditions of ingenious geometrical diagrams.

Self-evident as this is, it is not mentioned in Wetzel's frequently cited paper on the few-sided and many-sided pigmented cells of the retina. His conclusion as reported and apparently sanctioned by Schaffer is as follows:—

> Hätten alle Zellen den gleichen Wachstumsdruck, so müssten sie alle sechsseitige Form annehmen. Das Vorkommen der nicht sechsseitigen Formen kann durch gesteigerten Turgordruck für die siebenseitigen, verminderten für die fünfseitigen, allgemein aus den ungleichen biologischen Zuständen der einzelnen Epithelzellen verstanden werden.[14]

Gray's too cautious statement reads:—

> It must be admitted that there is no general agreement concerning the origin of those cells which exhibit more or less than six sides. . . . Cell division, cell growth, and cell absorption and fusion may well cause irregularities, but in no case has the actual process been seen under the microscope.[15]

Perhaps it can be generally agreed that whereas growth and shrinkage *may* cause changes in the number of cell contacts, they do not do

[14] Schaffer, J. Das Epithelgewebe. Hdb. d. mikr. Anat. d. Menschen, herausgegeben von W. v. Möllendorff, Bd. 2, Tl. 1, 1927, p. 13.
[15] Gray, J. Experimental Cytology, 1931, p. 257–258.

so necessarily. There is the collapsed fat cell figured in these Proceedings (vol. 61, Pl. 2, fig. 22) which retains 17 contacts, and the much shrunken cartilage cell (Pl. 2, fig. 19) with 13. Both of these cells show the markedly concave facets indicative of diminished turgor. An inordinately large fat cell, with decidedly convex walls, due to excessive turgor, has but 12 sides. Thus it appears that after certain labile stages the facets become firmly adherent and considerable changes in cell volume may occur without affecting their number. But in stratified epithelium, as the cells grow, they certainly gain facets at the expense of adjoining cells. To what extent this takes place in other tissues—the pigment layer, for example, or in cartilage—is a problem as interesting as it is difficult to determine. Curvature of the walls does not indicate that the few-faced cells are generally under diminished turgor, as compared with the many-faced. In none of these tissues, however, can cell division take place without altering the number of contacts of several cells. To deny cell division as a cause of differences in the number of facets is to deny its occurrence.

There is an important distinction between division in plane mosaics and in masses, in both cases, of course, avoiding 4-rayed intersections and tetrahedral angles. In the mosaic any division necessarily adds one cell and six sides, so that there is no possible deviation from the general average of six sides. In the mass of 14-hedra, however, the general average of 14 facets can be raised or lowered according to the number of sides in the plane of division. This may be readily visualized.

When a plane of division cuts through a polyhedral cell, it makes a new surface of mutual contact between the two daughter cells, thus creating two new facets. The division plane reaches the surface of the parental polyhedron and encircles it, cutting in two a varying number of facets, normally six. Each of these six is common to a surrounding cell, which exchanges its single facet of contact with the parent cell, for two facets of contact with the daughter cells. Accordingly the total number of facets added to the mass by any division is twice the number of facets in the division plane, plus two. When the plane is hexagonal, a new cell and a total of 14 facets are added. But if the division plane cuts off a trihedral corner of some cell, a tetrahedral cell is introduced, with the addition of 8 facets altogether. Such divisions would lower the general average of 14 facets, just as divisions through octagonal planes, for example, by adding one cell and 18 facets, would raise it. Since there is a tendency for large cells, which are many-faceted, to divide, we are interested in the latter

alternative. If the average number of facets in precartilage is 14, either the planes of division must be on the average hexagonal, or, if of higher average, there must be some compensating reducing factor such as 4-rayed intersections. The models include five pairs of cells in which the division planes may be studied.

It now appears that Leydig overstated the case when he said that sections of cartilage may look like fat *aufs Haar*. The cells of precartilage, but not of fat, are frequently in pairs and clusters as the result of division, and the pairs become evident on modeling. Some are separated by newly formed septa, characteristically large and thin. Others show thickening and contraction of the division plane until it becomes an ordinary facet, indistinguishable from the rest. Meanwhile the daughter cells grow unequally, since by divisions of adjacent cells, one may receive more facets than the other, and being diversely pulled about by surface tension, the pairs become unrecognizable.

Plate II, fig. 21 shows a pair of cells—a 14-hedron on the left and 12-hedron on the right—produced by the division of a 16-hedron. Parent and daughter cells have trihedral angles only. It is known that the polygons of a parent cell have a total of $6(n - 2)$ sides, and after division each daughter cell will have $6(n - 2)$ sides, but n is the same only in case of dividing cubes: usually there are two or three different values for n in this formula as applied to parent cell and the two daughters. The way in which the polygons covering the daughter cells come to have 12 less sides than if they were all hexagons, being in this respect like the parent, is as follows.

The total number of facets in the two daughter cells will be the number in the parent plus the number of sides in the division plane, plus 2. The 16-hedron in Plate II, fig. 21, might divide in a plane having any number of sides between 3 and 8. If the division plane were triangular, the daughter cells would have $16 + 3 + 2$ facets: but the plane is octagonal and the daughter cells have $16 + 8 + 2$ facets, or 26. With an octagonal division plane the daughter cells may be a pair of 13-hedra, or a 12- and 14-hedron as in the pair figured, or a more diverse combination totaling 26 facets.

From previous studies it is known that when the division plane cuts across a facet, it divides it into daughter facets which have 4 more sides than the parent. Plate II, fig. 21, shows a pentagonal, a hexagonal, and a heptagonal facet so divided. If x is the number of sides of the division plane which transects a polyhedron, $4x$ is the number of sides added to polygons on the exterior of the parent polyhedron, and $2x$ is the number of sides belonging to the two daughter poly-

hedra in their facet of mutual contact: $4x + 2x$, or $6x$, is the total addition in sides, but it is made by $x + 2$ facets. That is to say, the added facets have 12 less sides than if they were all hexagons. Since the parent cell already lacks 12 sides, there will be a total lack of 24. In the vertical bisection of an orthic tetrakaidecahedron oriented with a hexagonal facet above and below, an even apportionment of this deficit between the daughter cells is readily visualized. But also in the most unequal divisions, this deficit is shared alike. When a corner is cut from an orthic 14-hedron by a triangular division plane, the daughter cells have 4 and 15 facets respectively, with 12 and 78 sides,—in all cases $6(n - 2)$. In the irregular cells of the precartilage it is none the less inevitable, as exemplified in the pair shown in Pl. II, fig. 21. In agreement with the formula $6(n - 2)$ the polygonal facets of the 16-hedral parent must have a total of 84 sides; and the totals for the 14- and 12-hedral daughter cells must be respectively 72 and 60. The formula was established by counting the facets of these and similar cells and finding that such were the actual totals. It should be noted that the division plane cuts off quadrilateral facets, or, as in fig. 22, introduces triangular facets, *without any shrinkage of the adjacent cells*. Similarly division gives origin to heptagonal and octagonal facets of the neighboring cells, which need not enlarge to obtain them.

Plate II, fig. 22, is the model of a great cell with 20 facets, subdivided by a concavo-convex plane into daughters of very unlike shape but similar volume,—on the left, a 14-hedron of 55 c.c.; and on the right, a 15-hedron of 60 c.c. The plane of division is again octagonal. Just below the center of the figure, the plane passes quite exactly through a trihedral angle of the parent, thus forming an unstable tetrahedral angle, at the apex of a triangular facet of the 15-hedron. All other angles of the 15-hedron are trihedral, and its polygons therefore have 76 sides, being $6(n - 2)$ with a deduction of 2 for the tetrahedral angle. As the division plane extends from the triangular facet to the bottom of the figure, it coincides with the line of separation between two slender hexagonal facets of the parent. Since every parental facet is in contact with a separate adjoining cell, 4 cells are made to meet along this segment of the division plane. It will yield a 4-rayed intersection when cut across. This unstable feature accounts for the fact that the 20-faceted parent, dividing in an octagonal plane, produced daughter cells with a total of 29 facets instead of 30. Slight deviation of the plane to one side or the other would avoid the 4-rayed intersection and supply the missing facet. In other cases the division

plane coincides with an interfacial boundary through part of its extent and then leaves it, perhaps in process of eliminating the instability.

Three other pairs of recently divided cells have been modeled, in all of which the division plane is hexagonal. The parent cells have 14, 15, and 19 facets respectively, making the average for all five parental cells 16.8 facets. The ten daughter cells, with three lines of 4-rayed intersection, average 12.4 facets.

Tentative scheme of growth and division in precartilage cells.—In the foregoing fragmentary data, and the rough volume determinations, there is no inconsistency with an extension of the remarkable outcome of studies on the simple epithelium of the cucumber. It is here presented as a tentative possibility. In the interior of the precartilage of the tadpole the 14-hedron is then the average cell both in number of facets and in volume. At the enlargement used, 220 cells in section, without regard to their number of facets, occupied 3200 sq. cm., so that, if isodiametric, the average volume of a cell would be 55 c.c. Four of them were the 14-hedra modeled (Table III), which had an average volume of 60 c.c., but included a very large example. If the 14-hedron is the average both in facets and in volume, the average volumes of polyhedra with other numbers of facets must vary in arithmetical progression. The displacement measurements of our few models do not show what arithmetical progression exists, if any· but if it is like that clearly found in the epithelium of Cucumis, the 14-hedron should have an average volume of 12 units, and the average volumes of all other polyhedra should be two units less than their number of facets. In that event, the average end result of the division of any polyhedron in a hexagonal plane will be to add one cell, 12 units of volume, and a total of 14 facets to the mass. Accompanying such a division, six surrounding cells receive an added facet, and together grow 6 units, which is one-half of the volume to be added. The other half is supplied by the growth of the daughter cells, which together come to exceed the volume of the parent by 6 units. There are some reasons to suppose that the average number of facets of the dividing cells is 16. Such cells, if dividing equally in a hexagonal plane, would produce pairs of 12-hedra, and the average daughter cell in our series of ten has 12.4 facets. Not infrequently a large 14-hedron divides into a pair of 11-hedra. But if such a division should occur in a hypothetical mass composed entirely of 14-hedra, six of them would be changed to 15-hedra, becoming larger than the 14-hedra, and hence more likely to divide. But their division, in certain planes, adds to the sides of adjacent 15-hedra, making 16- and 17-hedra, with increasing

propensity toward division. The tentative conclusion that the average number of facets of dividing precartilage cells is 16, is by no means established by the data at hand. In the five pairs which were modeled, the average was 16.8; but it is quite possible that some of these cells had received an added side subsequent to their division into daughter cells, by the division of neighbors, and the probable error in so small a group is very high. The arithmetical progression in precartilage cells may well be a different one from that suggested; but that some equally definite ratio exists is the deduction from the foregoing study.

Intercellular spaces.—The resemblance between precartilage and vegetable parenchyma—Schwann's solid foundation for his cell theory—is primarily a matter of nuclear relations; but it depends also on the production of thin-walled 14-hedral units with a tendency to separate from each other at the corners and edges. There, in precartilage, the single line between adjacent cells splits in two, to enclose "a three or four-cornered intermediate space filled with a kind of homogeneous intercellular substance," of which there is not enough to yield gelatine on boiling.[16] In plants Amici had found that these spaces were not a casual laceration of the tissue, but were elegantly formed channels for conveying atmospheric air.[17] In fat, they lodge the vessels.[18] But these spaces are supposed not to exist in an aggregation of soap bubbles, and the physical factors which produce them have been described as quite abstruse.[19] In no other connection is a model made from rubber 'elastics' more instructive.

In Fig. 8, *A*, three elastics, *b*, *b*, *b*, of the same strength, each about 6 cm. long, have been looped around a shorter one, *a*, at equal intervals. In *B*, this combination of elastics has been stretched by slipping the three free loops over the thumb tacks *a*, *b* and *c*. These tacks have been inserted at equal distances from a central point, along lines diverging at angles of 120°. If we wish the three elastic rays, so constituted, to meet at the central point, they must be held there with pins, *d*, *e*, *f*. Remove the pins and a triangular intercellular space results (Fig. 8, *C*), the extent of which depends on the distance from the center that the walls are double. In Fig. 8, *B*, they are double from the center to *x*, *x'* and *x''*, and those points become the corners of the interspace. In regard to the tension in this system, I am indebted to Professor L. J. Johnson for the following memorandum:

[16] Schwann, Th. Untersuchungen. (Heft 1) 1838, p. 17, 18, 31.
[17] Amici, G. B. Osservazioni. Atti d. Soc. Ital. d. Sc. in Modena, 1823, T. 19, p. 47–48.
[18] Proc. Amer. Acad., 1925, vol. 61, p. 19.
[19] Gray, J. Experimental Cytology, 1931, p. 260–262.

Three 'rays', R, originally 120° apart, are subject to the same pull, P. Each pull, P, is resisted by the combined effect of the other two pulls, P. That effect not only balances P in line of R but at the same time makes a cross-wise or splitting effect on the material of R next the joint amounting to $0.866P$. After the material has opened at the joint under the influence of the pull of 0.866 P, and the resistance to the pull P in R is afforded by two forces 60° apart (instead of 120°), the cross-wise 'splitting' effect drops to 0.289 P. This means that if P were 100 grams in both cases, the cross-wise or splitting force would be 86.6 grams and 28.9 grams, in the 120° and the 60° cases, respectively.

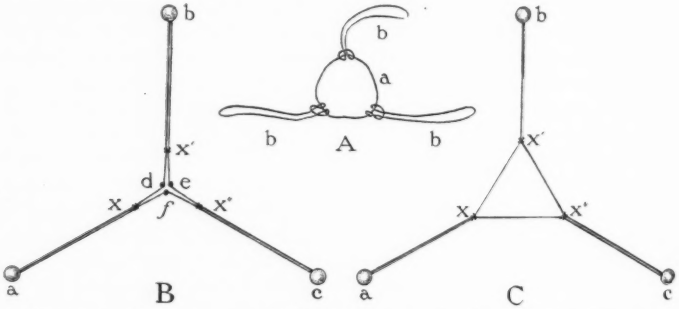


FIGURE 8. Arrangement of elastic loops showing that the tension where three rays meet tends to produce a triangular interspace.

Thus there is good reason for cell walls to split at the corners. Even if the cell is full of incompressible fluid, readjustments during growth allow this differential tension to express itself, producing little triangular interstices of the type seen in elder pith. An interstice of small size reduces the tension as much as a large one, and is made with almost inappreciable increase in the diameter of the cell. Accordingly, unless the substance within the space is under greater pressure than the cell contents, *small* triangular interstices may be expected. If these spaces follow the edges of massed 14-hedra, four of them become confluent at every trihedral corner, since a trihedral angle is obviously a place where four cells meet—the cell itself and three which are adjacent. A triangular prismatic space between the three adjacent cells will join three similar prismatic spaces which bevel the edges of any given polyhedral cell, meeting angle to angle. It is desirable to picture such a junction, though as Gray has said of Gibbs' ring,—"unfortunately the exact form of this area has not yet been shown to be susceptible to geometrical or mechanical definition."

Yet the general relations are absurdly simple, suggesting in our conventional model (Fig. 9) a hip roof and two chimneys.

The roof on the right of Fig. 9, in shape like an inverted V, is part of a quadrilateral facet of an orthic 14-hedron; the ridgepole runs between two hexagonal facets, and with the chimneys marks out three sides of a quadrilateral facet. Although in actual tissues the mutual inclination of the triangular prismatic spaces may differ widely from those of orthic 14-hedra, four of them will ordinarily meet at a corner, with an arrangement essentially like that of the model. There is no marked enlargement of the spaces at their confluence, so that in sections the distinction between a space along an edge and a space at

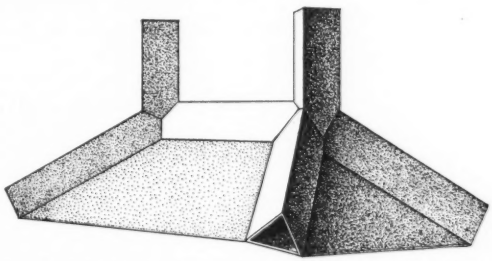


FIGURE 9. Model of triangular prismatic interspaces (*"edge spaces"*) following the edges of orthic 14-hedra.

a corner is not evident. Schaffer, in cartilage, calls them all *Zwickeln* or gussets, including under this term larger masses of matrix infiltrating degenerating cells.[20] From triangular intercellular gussets, hyaline matrix spreads over the entire surface of the cartilage cell, which thus loses its average 14-hedral shape, with 24 corners and 36 edges, becoming merely a rounded cell lodged in a spheroidal lacuna. In other tissues the intercellular spaces have more complex and engrossing relations. How some classic examples are related to the primary 14-hedral shape of cells in masses may be reviewed in conclusion.

When the contents of the intercellular space, whether air or liquid, is under less pressure than the contents of the cell, it is expected that the triangular intercellular spaces will have concave sides, as in elder pith and countless other examples. But if the pressure in the space exceeds that in the cell, the triangular prismatic interspace becomes cylindrical, and in section may spread out as a lake (Fig. 10, *A*, at *x*). Over the facets of the cell, tension of the walls acts against separation,

[20] Von Möllendorff's Handbuch, Bd. 2, Tl. 2, Abb. 106 and 108, on p. 148 and 150.

as seen in the close approximation of the two sides of the elastic loop in each ray of Fig. 8, *C*. But beads of excreted air or other substance may overcome this tension, forcing the walls apart in little blebs (Fig. 10, *A*). They may expand more readily toward the fluid interior of the cell than laterally in the crusta, thus becoming perpendicular ellipsoids, as in Meyen's old drawing of Sagittaria (Fig. 10, *B*). On surface view the cell membrane over the facet of such a cell appears coarsely perforated by circular vacuolar pits, into which, however, it descends, thinned but without interruption. A peripheral condensation of the cytoplasm would account also for the reversed orientation of the triangular prismatic spaces which follow the polyhedral edges. Instead of presenting sides toward the cytoplasm as in elder pith, these sides, after being pushed into the cells, have become the angles of the triangular space.

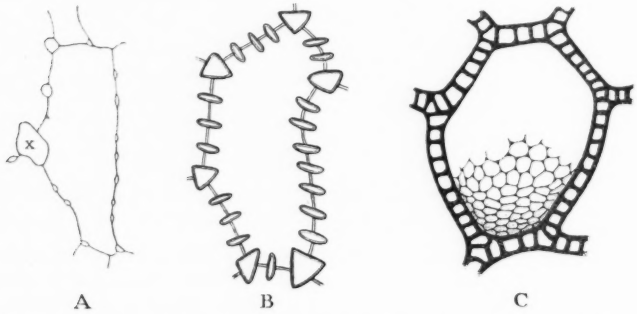


FIGURE 10. *A*, a cell with adjoining interspaces, from the stem of *Scirpus validus*. L. M. Snow (*Bot. Gaz.*, 1914, vol. 58, p. 507, fig. 10). *B*, cell with adjoining interspaces, from the leaf-stalk of *Sagittaria indica*. F. J. F. Meyen (*Pflanzen-Physiologie*, 1837, Bd. 1, Tab. 2, fig. 9). *C*, cell with adjoining interspaces from the stomach of a cow embryo of 30 cm. M. Ide (*La Cellule*, 1888, T. 4, following p. 432, fig. 5).

In the prickle cells of animals (Fig. 10, *C*, from Ide's noted paper), numerous and closely crowded intercellular vacuoles such as Meyen figured in Sagittaria, have become confluent. They coalesce around the vertical strands where three of them meet, and these strands persist as intercellular bridges. The vacuoles communicate also with the triangular spaces which follow the edges of the polyhedral cells. At the base of the bridges or prickles, Ide observed a reticulate cell membrane, shown in surface view in the lower half of his figure. The

prickles extend upward from the thickened nodal points in this net. They are only "des dépendances de la membrane cellulaire, des portions de la membrane primitivement simple qui persistent et s'allongent après son clivage."[21] Ide emphatically denies that the bridges are protoplasmic processes withdrawn and sent forth like the pseudopods of an amoeba.

Although the cupped ends of the intercellular vacuoles would produce such a reticular membrane as Ide described, depending chiefly on late enbryos, there is no trace of it in a finely preserved block of tissue from the adult cervix uteri for which I am indebted to Dr. Shields Warren.[22] In this uterine epithelium, with the stain used,

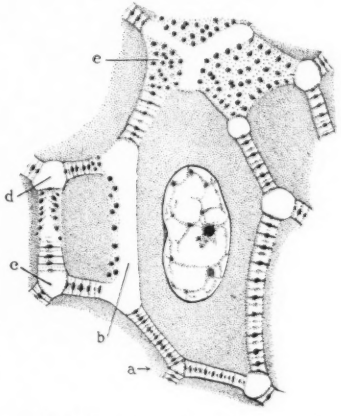


FIGURE 11. Intercellular edge-spaces following the edges of the cell facets, and interfacial spaces crossed by bridges, in the normal epithelium of the cervix uteri from a woman of 55 years. 3 μ section, Mallory's phosphotungstic acid haematoxylin. × 2600 diam.

nothing is seen of the much studied 'tonofibrils.' But the neglected system of spaces following the polyhedral edges is shown clearly. At *c* and *d* in Fig. 11 one may look down the chimneys of an arrangement of canals like that in Fig. 9. The connecting ridgepole, however, is

[21] Ide, M. La membrane des cellules du corps muqueux de Malpighi. La Cellule, 1888, T. 4, p. 425.

[22] Shaffer figures the reticular membrane in the epidermis from a man of 20 (Abb. 28 in von Möllendorff's Hdb., Bd. 2, Tl. 1, p. 33), yet in two inconsistent ways, without comment: he places the bridges in the centers of the meshes in one part of the figure; and, like Ide, at the nodal points in another part of the same figure.

bounded by transverse bridges across its top, and converging bridges along its sides. For, owing to the development of the interfacial layer of communicating vacuoles, the three simple cell membranes, which met at angles of approximately 120°, have each been split into a pair of parallel membranes meeting at the same angle, the membranes of each pair retaining connection with each other by perpendicular bridges. Hence the triangular interspace, bounded by bridges, has the reversed orientation (Fig. 11, *a*). But many of these spaces are distended and round, the cell bridges preventing so wide a separation over the facets as occurs at the edges and corners. At *b* an edge-space is cut lengthwise and shows no special enlargement at its junction with other canals.

The primary system of channels which follow the edges should be more carefully distinguished from the secondary interfacial spaces than has been done, for example, in Flemming's study of the branchial epithelium of the salamander. Apparently Flemming considers that leucocytes may wander through both sorts of spaces, and Wilson interprets his guarded statements and dubious drawings to mean that "they rupture the plasma-bridges which are then formed anew behind them."[23] In the uterine epithelium—at least in a hundred instances examined for the purpose—I found that the leucocytes had forced their way into the edge-canals, stretching, but not rupturing, the adjacent bridges: they were never in the interfacial spaces.

The bridges are somewhat irregularly distributed as they rise from the surface of a facet (Fig. 11, *c*). Their considerable increase in number as the cell enlarges and moves to the outer strata, comes evidently from the splitting of those already present: no pseudopodial outgrowths were observed. The prickle cell is therefore typically a 14-hedral object, with canals along its 36 edges, and with facets beset with a large number of prickles, or simple short branches, due to the coalescence of a layer of interfacial vacuoles.

If the confluent vacuoles should extend further into the cell, decreasing in number as they approach the nucleus, the processes would unite in a ramifying system, converging toward the center of the 14-hedral territory. In sclerenchyma (Fig. 12) the same thing takes place *within* the cell. The cell outlines are certainly those of 14-hedra (on the average), showing minute intercellular spaces at many edges and corners. But the shape of bone cells is more difficult to determine,

[23] Flemming, W. Über Intercellularlücken des Epithels. Anat. Hefte, Abth. 1, 1895, Bd. 6, p. 10–11; Taf. 1, Fig. 1–2. Wilson, E. B. The Cell. 3d ed., 1925, p. 106.

since the deposit of bone is outside the cells, and there are no cell walls, —the branching processes show no such nodes as conveniently mark the limits of the unbranched processes of the prickle cells. The problem may be approached, however, for it would be solved by combining, in three-dimensional form, two such sections as are shown in Fig. 13, *A* and *B*. *A* is the shape of bone cells in tangential view of the Haversian system; and like cork cells in tangential section of the tree trunk, the average territory of the cell tends to be a regular hexagon. This territory in the bone cell includes the processes of a given cell, and is similar to the branching cell territory in the peach stone. But

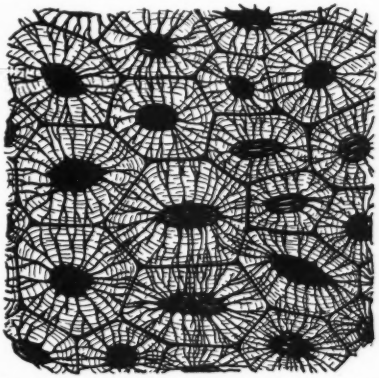


FIGURE 12. Sclerenchyma. Stone cells in a section of a peach stone. E. C. Jeffrey (*Anatomy of Woody Plants*, 1917, p. 4, fig. 3. Courtesy of the Univ. of Chicago Press).

when the Haversian system—or the tree trunk—is bisected longitudinally, so as to produce a radial section, the average shape of a cell territory is a *rectangular* hexagon (Fig. 13, *B*). Transverse sections of Haversian system and tree trunk are similar to the radial sections. Hence we conclude that the branching bone cells in relation to the Haversian system (and in the periosteal lamellae, in relation to the shaft of the bone) are oriented like the simple cork cells in relation to the tree trunk. Like the latter they are then, on the average, 14-hedral.[24]

In the development of the bone cells in Fig. 13, *A*, we may assume a corresponding layer of osteoblasts in the plane of the page, each in

[24] Lewis, F. T. The shape of cork cells. Science, 1928, vol. 68, p. 625–626.

relation, on the average, with six others laterally. These osteoblasts deposit bone in confluent interfacial vacuoles on one side of the cell only (which is in the plane of the page), and the layers of bone so deposited, penetrated by the lengthening vertical bridges, will lift the osteoblasts above the page. At various levels, an osteoblast becomes imbedded in the matrix, selected presumably by its spatial relations to those already imbedded. It is then flattened out in a tangentially radiating pattern, receiving its parallel vertical processes at right angles. Presumably it is active in the formation of the additional laminae of bone, parallel with the first set, which now form on the

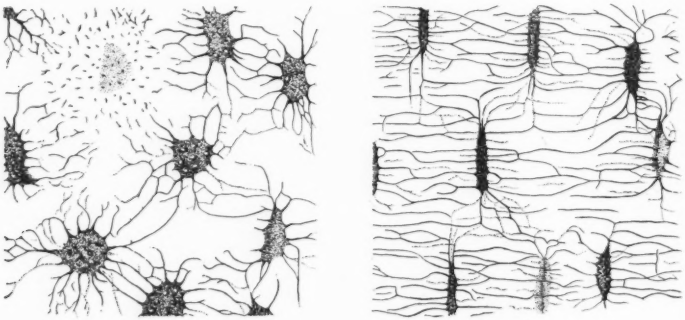


FIGURE 13. *A* and *B*, two longitudinal sections of bone cells, from one and the same Haversian system in a human humerus. × 500 diam. The Haversian canal is vertical in relation to the drawing. *A*, tangential section: *B*, radial section. These patterns are consistent with an average 14-hedral cell territory, in which case the orientation of the bone cells in relation to the Haversian canal is like that of cork cells in relation to the tree trunk.

opposite or upper side of the cell and contain another set of vertical processes; but unfortunately, as already noted, the processes show no line of nodes to indicate the cell boundary. Otherwise comparison between the bone cells (Fig. 13, *A*) and the prickle cells (Fig. 11) may readily be made, even though the interfacial vacuoles in bone have become very extensive. There are strips of bony matrix free from canaliculi which seem to represent the edge-canals.

In mesenchyma there are both extracellular and intracellular vacuoles, the latter apparently breaking through to the exterior so that the 14-hedral cells become very irregularly radiate. Yet the territory controlled by a nucleus is presumably on the average 14-faced, as is

certainly true of the stellate parenchyma of Juncus. In the pith of Juncus no intracellular vacuoles split its cytoplasm into shreds, and there are usually no extracellular vacuoles other than those which follow the edges of the cell. Hence the 14-hedral cell becomes primarily a 14-rayed star. Two of these rays which, on connecting with others, form continuous vertical strands up and down the pith, early disappear.[25] Suspecting that they were mechanically superfluous in resisting the lateral swaying of the stem, and otherwise unable to suggest why these two rays should sever and retract, whereas all the others are well represented, I submitted the question to the civil engineer, and received from Professor L. J. Johnson the following reply:—

> The presence of the firm vertical casing of Juncus—the casing being a stiff ring in cross-section—seems to me to leave no mechanical reason for vertical strands in the pith. The zig-zag strands of webbing, together with the horizontal discs, form a sufficiently firm sponge to support the relatively slight vertical load and carry it to the external walls of the Juncus.

But the fact that the vertical rays are functionless is only further incentive to study the mechanics of their elimination. If growth were equal in all directions, there would be no reason why one ray should rupture rather than another (except that the rays are of two diameters and lengths, six of the fourteen being somewhat longer and thinner than the other eight). But the rush does not expand equally. It grows tall and slender, and the special tension on the vertical strands accounts for their rupture. Their stumps are then withdrawn into the central nucleated discs which are stretched laterally by the remaining rays, all of them coming to rest at angles approaching 120°. This deduction, however, rests on computations, quite beyond the author's ability, generously supplied by Professor Johnson and his assistant Mr. F. J. Mardulier. Their memorandum is as follows:—

> Since vertical growth is greater than lateral growth, the main stress on the cell is that due to vertical forces which can be indicated by the force T in the diagram, Fig. 14. This force T must be resisted by the pull on the top face and the vertical components of the pulls on the six adjacent oblique faces. Hence we obtain the statical equation:
>
> $$T = P + 3Q \sin \alpha + 3R \sin \beta$$
>
> The magnitudes of P, Q and R can be determined by the aid of the principle of least work, *i. e.* the magnitudes of P, Q and R must be such as will make the work done in elongating their respective rays a minimum.

[25] Proc. Amer. Acad., 1925, vol. 61, p. 10–11.

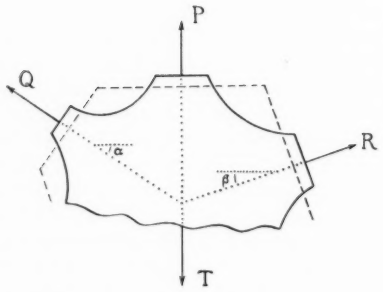


FIGURE 14. Diagram (drawn by F. J. Mardulier) of forces which rupture the vertical rays of the cells in Juncus pith. In heavy lines, a portion of a developing stellate cell; in dashes, the corresponding part of the orthic 14-hedron from which it was derived.

Hence, using Ap, Aq, Ar for the respective areas of the cross sections of the rays P, Q and R, and Lp, Lq, Lr for the respective lengths of the rays P, Q and R, the magnitudes of the forces P, Q and R are found to be as follows:

$$P = \frac{T}{1 + 3\frac{Lp}{Lr} \cdot \frac{Ar}{Ap} \cdot \sin^2 \beta + 3\frac{Lp}{Lq} \cdot \frac{Aq}{Ap} \cdot \sin^2 \alpha}$$

$$Q = \frac{T \sin \alpha}{\frac{Lq}{Lp} \cdot \frac{Ap}{Aq} + 3\frac{Lq}{Lr} \cdot \frac{Ar}{Aq} \cdot \sin^2 \beta + 3 \sin^2 \alpha}$$

$$R = \frac{T \sin \beta}{\frac{Lr}{Lp} \cdot \frac{Ap}{Ar} + 3\frac{Lr}{Lq} \cdot \frac{Aq}{Ar} \cdot \sin^2 \alpha + 3 \sin^2 \beta}$$

If we take dimensions from the schematic wax reconstruction of the developing stellate cell (such as is figured in these Proceedings, vol. 61, p. 8, fig. 6), which we are justified in doing since the various dimensions enter the equations in the form of ratios only, we get the values: $P = .250T$, $Q = .204T$, and $R = .145T$. Hence $P = 1.23Q$, and $P = 1.73R$. In other words, the vertical rays of the cell bear the brunt of the vertical attack, and the other rays bear smaller tensions as their angle of inclination to the horizontal decreases. Accordingly the vertical rays break.

This eminently satisfactory outcome in connection with a tissue of diagrammatic simplicity gives reason to believe that a further study

of bone and mesenchyma by the same methods will be correspondingly illuminating. For the present we can give only a tentative negative answer to the fundamental question whether protoplasmic processes in mesenchyma branch out through the intercellular spaces and make connections with cells beyond the 14-hedral limits. Whether leucocytes in leaving the endothelial tubes elect the points where three cells meet, which are mechanically the places of least resistance, and whether the transformation of endothelium into reticular tissue occurs by the enlargement of spaces at such points, must be subjects for further study. The morphology of reticular tissue is unfortunately unknown.

A surmise concerning nerve cells and neuroglia.—Out of the primitive uniformity of the walls of the medullary tube there arise two types of branching cells;—the morphological problem of their origin is the subject of this surmise. Since cells formed around nuclei distributed at random are on the average 14-hedral, it may be assumed that the primitive cells of the medullary tube are of this character. Though the preceding study of cartilage has shown what diverse forms may be expected under that generalization, a diagrammatic model, in which the primitive cells of the medullary tube are all orthic 14-hedra, is nevertheless serviceable. As in other tissues, intercellular spaces will doubtless develop most readily along the edges of the facets. Further, I would utilize the *verdienstvolle Untersuchungen* of two of my early Harvard teachers,—Davenport, who found that in tadpoles growth is chiefly the result of the "differential imbibition of water," and Schaper, who recognized that there are two cytological types of this imbibition,—intracellular, and intercellular. The former gives to precartilage cells the turgor requisite for their functional rigidity, and incidentally a plump polyhedral form: the latter loosens mesenchyma and makes its cells stellate.[26] If this is true, I would suggest that in the wall of the medullary tube both processes occur simultaneously. Nerve cells imbibe and grow by sending out processes, perhaps at the expense of the neuroglia cells. The latter become relatively shrunken, behaving like cells of Juncus pith. The processes of the nerve cells would grow out where the resistance of the surrounding cells is least, and in making their way between the neighboring cells they would follow the paths of least resistance. That is to say, they would grow

[26] Davenport, C. B. The rôle of water in growth. Proc. Boston Soc. Nat. Hist., 1897, vol. 28, p. 73–84. Schaper, A. Beiträge zur Analyse des thierischen Wachsthums. Tl. 1. Arch. f. Entw.-Mech., 1902, Bd. 14, p. 376–381. Schaffer in his admirable presentation of cartilage already cited commends these papers.

out from the corners of the nerve cells, and would extend through the little intercellular spaces following the edges of the facets. It is easy to make a hypothetical model on these specifications and see if it at all resembles nerve tissue.

In a mass of orthic tetrakaidecahedra, let one become a nerve cell, sending out a primary process or neuraxon from one corner, and

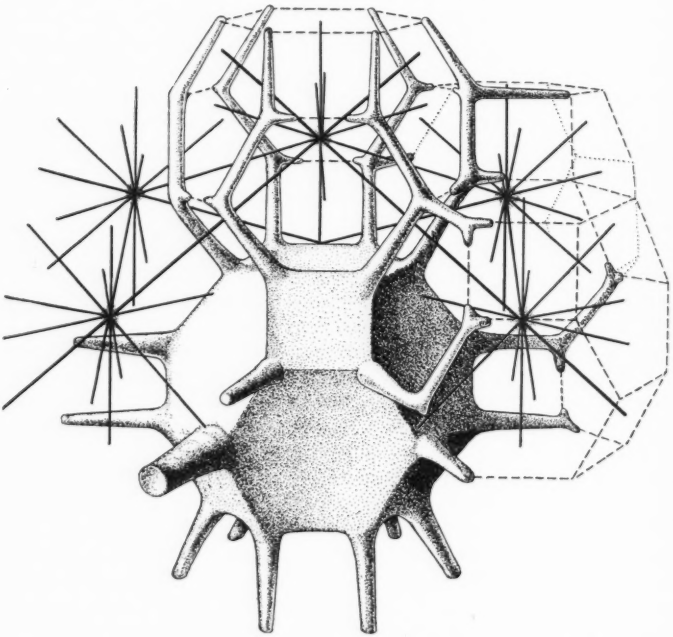


FIGURE 15. Schematic model based upon six orthic tetrakaidecahedra in contact with one another. One of the six, in the manner of a nerve cell, has sent out processes from all its corners and they extend through intercellular edge-spaces. The other five, perhaps like neuroglia, are reduced to radiate form by the enlargement of the intercellular edge-spaces. Since the ray to the nerve cell has been omitted, each of the five has 13 rays.

secondary processes or dendrites from all other corners, and let them follow the interstitial spaces. Rather than bifurcate, the dendrites would trifurcate, or have opportunity so to do. There is, however, no

necessity for taking advantage of all these opportunities, nor for the nerve cell to produce its full quota of $2n - 4$ processes. It may be unipolar or bipolar; but in the model, Fig. 15, the shaded body is a 14-hedron which has sent out processes from every corner,—one neuraxon and 23 dendrites.

The relative abundance of nerve cells and neuroglia in the medullary tube, and their relation to one another, should be known before proceeding with the schematic model. If a nerve cell is not completely surrounded by neuroglia, it would be expected to retain interfacial contacts with one or more nerve cells, and such contacts could be drawn out into thick processes extending from nerve cell to nerve cell. Luys figured this sort of thing plainly enough in '65, but neurologists of later date do not recognize it.[27] Certainly no process of a nerve cell goes out to join a process from a glia cell, end to end. Thus it appears that neuroglia withdraw from their original interfacial connection with nerve cells, while retaining such connection with other neuroglia. Then, if the primary intercellular spaces along the edges of the facets greatly enlarge with the growth of the tissue, the glia cells make a net-work comparable with that in Juncus pith, though differing in detail. Five such cells are shown in the model. If nerve cells are completely surrounded by glia cells, there will be five per nerve cell in what seems the most compact arrangement.

On the right of the model the outlines of the original 14-hedra are shown in dashes; and within them, in solid lines, are the 13-rayed neuroglia to which they have given rise. The 14th ray, which would run to the nerve cell, has been omitted. Each ray of the glia cell extends from the center of the primitive 14-hedron which produced it, to the center of one of its facets, and thence is continued directly by the ray of an adjoining glia cell. Fibers developed along or in these rays may pass straight from one cell territory to another. Many rays doubtless rupture and disappear; others may split secondarily, so that the pattern postulated is consistent with as great a degree of irregularity as that actually observed in nerve tissue.

On the left of the model, there are two glia cells, quite like those on the right, except that the 14-hedral territory from which they were derived is not indicated. With the stellate regression of the neuroglia, the intercellular spaces become so large that the dendrites would not preserve the angular kinks, which are perhaps the most unnatural feature of the model.

[27] Luys, J. Recherches sur le système nerveux. Paris, 1865. Atlas, Pl. 19, fig. 1.

The nerve cell is formed for a purpose which would be defeated by cell division, and division does not occur. Although the size of the motor cells and of their nuclei is such that if found in other tissues division would surely be expected, the dendrites are not to be separated from their neuraxon and the mechanism wrecked by division. In stellate neuroglia, division would have the effects previously described in Juncus pith, reducing the radiations per cell. It is presumably very infrequent. Proliferation yielding unbranched polyhedra, which subsequently become stellate, would account for the new formation of neuroglia of more normal pattern. In the growth of the medullary tube, cell division in both nerve cells and neuroglia is presumably in the unbranched polyhedral stage of development.

The model shows, at least, the possibility of deriving the nervous system from an aggregate of cells which on the average are 14-hedra. It indicates a more radical difference between the aggressive nerve cells and the regressive neuroglia than the stellate shape of both might suggest. But it is at present a surmise, awaiting the actual morphological reconstruction of a block of nerve tissue by some one who can carry Cajal's studies a step further.

EXPLANATION OF PLATES.

PLATE I.

FIGURE 16. Wax plate reconstruction of a group of 17 precartilage cells. From the mandibular cartilage of a 25-mm. tadpole of *Bufo lentiginosus*. × 800 diam.

PLATE II.

Wax reconstructions of individual precartilage cells included in the group in Plate I (with an additional cell in Figure 17). × 900 diam.

FIGURE 17. Typical 14-hedral cell.

FIGURE 18. 14-hedron with two tetrahedral angles.

FIGURE 19. Laterally compressed cell with 13 facets.

FIGURE 20. Large cell with 21 facets

FIGURE 21. 14-hedron (left) and 12-hedron (right) produced by the division of a 16-hedron.

FIGURE 22. 14-hedron (left) and 15-hedron (right) produced by the division of a 20-hedron.

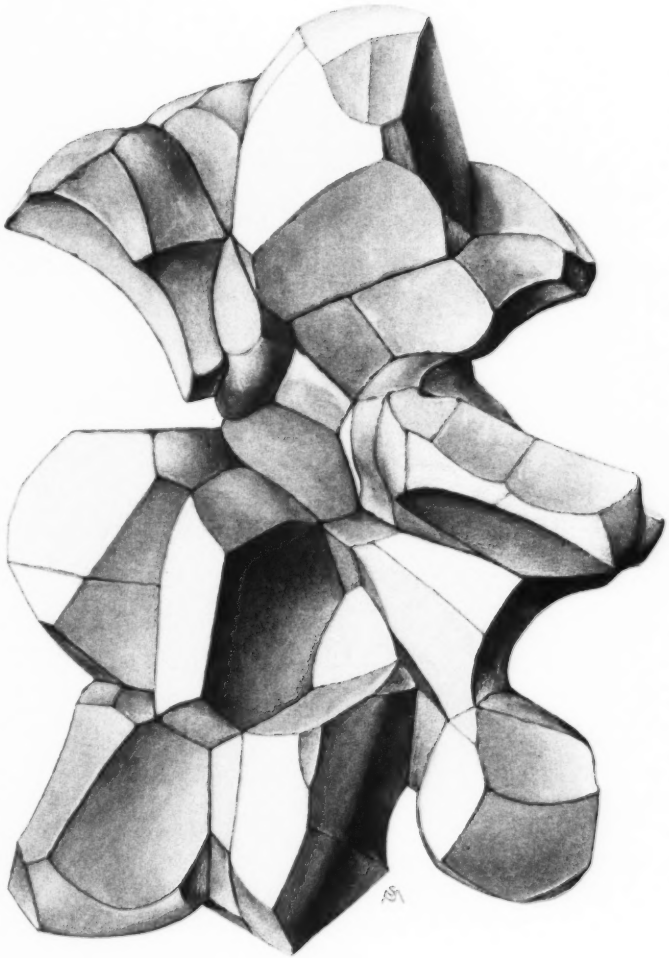


FIG. 16

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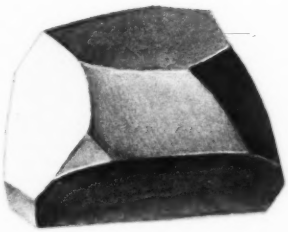

FIG. 17

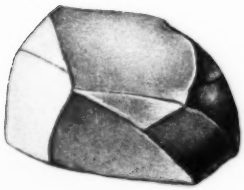

FIG. 18

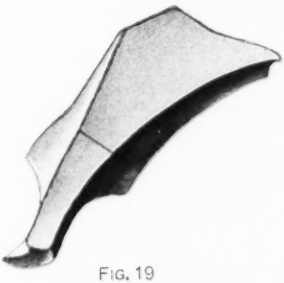

FIG. 19

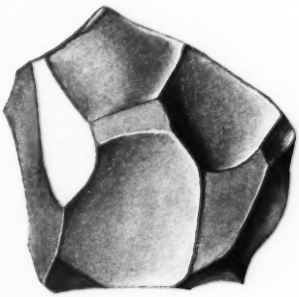

FIG. 20

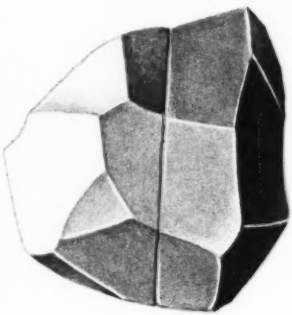

FIG. 21

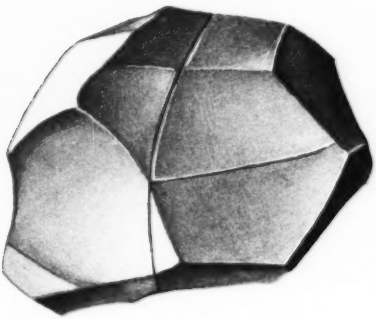

FIG. 22

F. S. M. Del.

THE HELIOTYPE CORP. BOSTON